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Date: August 10, 2005

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AUG 1 1 2005

## IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Application of: Akiyama et al. Examiner: Unassigned

Application No.: 10/537,001

Group Art Unit: Unassigned

May 20, 2005 Filed:

Confirmation No.:

Unassigned

Docket No.:

3190-078

Customer No.:

33432

For:

COLON CANCER METASTASIS INHIBITOR

## INFORMATION DISCLOSURE STATEMENT PURSUANT TO 37 CFR 1.97(b)

Mail Stop Amendment Commissioner for Patents P.O. Box 1450 Alexandria, VA 22313-1450

August 10, 2005

Sir:

The attention of the Patent and Trademark Office is hereby directed to the documents listed on the attached Form PTO/SB/08. Pursuant to the current United States Patent and Trademark Office rules, no copies of U.S. Patents/Patent Application Publications are provided.

This Information Disclosure Statement is being submitted before expiration of the threemonth period following filing of the above-captioned application.

The above information is presented so that the Patent and Trademark Office can, in the first instance, determine any materiality thereof to the claimed invention. See 37 CFR 1.104(a) and 1.106(b) concerning the PTO duty to consider and use any such information. It is respectfully requested that the information be expressly considered during the prosecution of this application, Information Disclosure Sment U.S. Patent Application No. 10/537,001

and that the documents cited in the attached Form PTO/SB/08 be made of record therein and appear on the first page of any patent to issue therefrom.

This submission does not represent that a search has been made or that no better art exists and does not constitute an admission that each or all of the listed documents are material or constitute "prior art." If the Examiner applies any of the documents as prior art against any claim in this application and applicant determines that the cited documents do not constitute "prior art" under United States law, applicant reserves the right to present to the office the relevant facts and law regarding the appropriate status of such documents.

Applicant further reserves the right to take appropriate action to establish the patentability of the disclosed invention over the listed documents, should one or more of the documents be applied against the claims of the present application.

It is believed that no fee is required to make this a complete and timely filing. However, if it is determined that a petition or fee is required, the Commissioner is hereby authorized to charge any fee associated with this statement to our Deposit Account No. 50-0925.

Respectfully submitted,

Luke A. Kilyk

Reg. No. 33,251

Atty. Docket No.: 3190-078

KILYK & BOWERSOX, P.L.L.C.

53 A East Lee Street Warrenton, VA 20186

Tel.: (540) 428-1701

Fax: (540) 428-1720

Enclosures: PTO-SB-08, w/22 Documents

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Filing Date	May 20, 2005					
First Named Inventor	AKIYAMA et al.					
Art Unit	Unassigned					
Examiner Name	Unassigned					
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Complete if Known Substitute for form 1449A/PTØ AUG 1 1 2005 Application Number 10/537,001 Filing Date May 20, 2005 INFORMATION DISCLOSURE First Named Inventor AKIYAMA et al. STATEMENT BY ARPLICAN Art Unit Unassigned (use as many sheets as necessar) **Examiner Name** Unassigned Sheet of Attorney Docket Number 3190-078

NON PATENT LITERATURE DOCUMENTS								
Examiner Initials*	Cite No.1	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date page(s), volume-issue number(s), publisher, city, and/or country where published.	T²					
		KAWASAKI et al., "Mutated APC and Asef are Involved in the Migration of Colorectal Tumor Cells," NATURE CELL BIOLOGY, Vol. 5, March 2003 (pgs. 211-215).						
		JIMBO et al., "A New Stage of a Study of APC Protein," MOLECULAR MEDICINE, Vol. 39, No. 11, 2002 (pgs.						
		1274 - 1279) (with partial English translation).						
		AKIYAMA, "The Tumor Suppressor Gene Product APC and Asef," JOURNAL OF CLINICAL AND EXPERIMENTAL						
		MEDICINE, Vol. 205, No. 13, 2003 (pg. 1001) (with partial English translation).						
		KAWASAKI et al., "A Mutated APC/Asef Complex is Involved in Motility of Cololectal Cancer Cells,"						
		SUPPLEMENT OF JAPANESE JOURNAL OF CANCER RESEARCH, No. 3048, Vol. 61, 2002 (pg. 111) (with partial						
		English translation).  KAWASAKI et al., "Asef, a Link Between the Tumor Suppressor APC and G-Protein Signaling," SCIENCE,						
		KAWASAKI et al., "Aset, a Link Between the Tumor Suppressor APC and G-Protein Signaling," SCIENCE, Vol. 289, August 18, 2000 (pgs. 1194-1197).						
		KAWASAKI et al., "A Novel Function of the Tumor Suppressor Gene Product APC," PROTEIN, NUCLEIC						
		ACID AND ENZYME, Vol. 46, No. 3, 2001 (pgs. 228-232) (with partial English translation).						
		SENDA, "APC Tumor Suppressor Gene Diversity of its Expression and Functions," JPN. J. CLIN.						
		ELECTRON MICROSC., Vol. 33, No. 2, 2001 (pgs. 65-74) (with partial English translation).						
		PADDISON et al., "Short Hairpin RNAs (shRNAs) Induce Sequence-Specific Silencing in Mammalian						
		Cells," GENES & DEVELOPMENT, Vol. 16, No. 8, 2002 (pgs. 948-958).						
		JENUWEIN, "An RNA-Guided Pathway for the Epigenome," SCIENCE, Vol. 297, September 27, 2002 (pgs.						
		2215-2218).						
		KINZLER et al., "Lessons from Hereditary Colorectal Cancer," CELL, Vol. 87, October 18, 1996 (pgs. 159-170)						
		FEARNHEAD et al., "The ABC of APC," Human Molecular Genetics, Vol. 10, No. 7, 2001 (pgs. 721-733).						
		BIENZ et al., "Linking Colorectal Cancer to Wnt Signaling," CELL, Vol. 103, October 13, 2000 (pgs. 311-320).						
	PEIFER et al., "Wnt Signaling in Oncogenesis and Embryogenesis A Look Outside the Nucleus," SCIENCE, Vol. 287, March 3, 2000 (pgs. 1606-1609).							
	AKIYAMA, "Wnt/β-Catenin Signaling," CYTOKINE & GROWTH FACTOR REVIEWS, Vol. 11, 2000 (pgs. 273-282).							
		MIYOSHI et al., "Somatic Mutations of the APC Gene in Colorectal Tumors: Mutation Cluster Region in the APC Gene," HUMAN MOLECULAR GENETICS, Vol. 1, No. 4, 1992 (pgs. 229-233).						
		NAGASE et al., "Mutations of the APC (Adenomatous Polyposis Coli) Gene," HUMAN MUTATION, Vol. 2,						
		1993 (pgs. 425-434).						
		MOLENAAR et al., "XTcf-3 Transcription Factor Mediates β-Catenin-Induced Axis Formation in Xenopus						
		Embryos," CELL, Vol. 86, August 9, 1996 (pgs. 391-399).						
		BEHRENS et al., "Functional Interaction of β-Catenin With the Transcription Factor LEF-1," NATURE, Vol. 382, August 15, 1996 (pgs. 638-642).						
		WONG et al., "Forced Expression of the Tumor Suppressor Adenomatosis Polyposis Coli Protein Induces						
		Disordered Cell Migration in the Intestinal Epithelium," PROC. NATL. ACAD. SCI, USA, Vol. 93, September						
		1996 (pgs. 9588-9593).						
	OSHIMA et al., "Morphological and Molecular Processes of Polyp Formation in Apc <sup>Δ/16</sup> Knockout Mice," CANCER RESEARCH, Vol. 57, May 1, 1997 (pgs. 1644-1649).							
	International Search Report for PCT/JP03/10449 dated December 2, 2003.							
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